

CLAIMS

We claim:

1. A targeting construct comprising:
 - 5 (a) a first polynucleotide sequence homologous to a BMP gene;
 - (b) a second polynucleotide sequence homologous to the BMP gene; and
 - (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
- 10 3. A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to a BMP gene;
 - (b) providing a second polynucleotide sequence homologous to the BMP;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a
 - 15 vector, to produce the targeting construct.
4. A method of producing a targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first
 - region of a BMP gene and a second sequence homologous to a second regchange
 - cross references to hard numberscion of a BMP gene;
 - 20 (b) inserting a positive selection marker in between the first and second sequences
 - to form the targeting construct.
5. A cell comprising a disruption in a BMP gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
- 25 8. A non-human transgenic animal comprising a disruption in a BMP gene.
9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in a BMP gene,
the method comprising:
 - (a) introducing the targeting construct of claim 1 into a cell;
 - 30 (b) introducing the cell into a blastocyst;

- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
 - (d) breeding the chimeric mouse to produce the transgenic mouse.
11. A method of identifying an agent that modulates the expression of a BMP, the
5 method comprising:
 - (a) providing a non-human transgenic animal comprising a disruption in a BMP gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the expression of BMP in the non-human transgenic
10 animal is modulated.
12. A method of identifying an agent that modulates the function of a BMP, the method comprising:
 - (a) providing a non-human transgenic animal comprising a disruption in a BMP
15 gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the function of the disrupted BMP gene in the non-human transgenic animal is modulated.
13. A method of identifying an agent that modulates the expression of BMP, the
20 method comprising:
 - (a) providing a cell comprising a disruption in a BMP gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether expression of the BMP is modulated.
14. A method of identifying an agent that modulates the function of a BMP gene, the
25 method comprising:
 - (a) providing a cell comprising a disruption in a BMP gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether the function of the BMP gene is modulated.
15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.
- 30 16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a BMP gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: kinky tail, low body weight, or short body length.
18. A method of producing a transgenic mouse comprising a disruption in a BMP gene,
5 wherein the transgenic mouse exhibits at least one of the following phenotypes: kinky tail, low body weight, or short body length, the method comprising:
 - (a) introducing a BMP gene targeting construct into a cell;
 - (b) introducing the cell into a blastocyst;
 - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said
10 pseudopregnant mouse gives birth to a chimeric mouse; and
 - (d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a BMP gene.
19. A cell derived from the transgenic mouse of claim 17 or claim 18.
20. A method of identifying an agent that ameliorates a phenotype associated with a
15 disruption in a BMP gene, the method comprising:
 - (a) administering an agent to a transgenic mouse comprising a disruption in a BMP gene; and
 - (b) determining whether the agent ameliorates at least one of the following phenotypes: kinky tail, low body weight, or short body length.
- 20 21. A method of identifying an agent that modulates BMP expression, the method comprising:
 - (a) administering an agent to the transgenic mouse comprising a disruption in a BMP gene; and
 - (b) determining whether the agent modulates BMP expression in the transgenic
25 mouse, wherein the agent has an effect on at least one of the following phenotypes: kinky tail, low body weight, or short body length.
22. A method of identifying an agent that modulates a phenotype associated with a disruption in a BMP gene, the method comprising:
 - (a) administering an agent to a transgenic mouse comprising a disruption in a
30 BMP gene; and

(b) determining whether the agent modulates at least one of the following phenotypes: kinky tail, low body weight, or short body length of the transgenic mouse.

23. A method of identifying an agent that modulates BMP gene function, the method comprising:

- (a) providing a cell comprising a disruption in a BMP gene;
- (b) contacting the cell with an agent; and
- (c) determining whether the agent modulates BMP gene function, wherein the agent modulates a phenotype associated with a disruption in a BMP gene.

24. The method of claim 23, wherein the phenotype comprises at least one of the following: kinky tail, low body weight, or short body length.

25. An agent identified by the method of claim 20, claim 21, claim 22, or claim 23.

26. An agent that modulates the activity of a BMP gene.

27. A method of ameliorating a disorder associated with a mutation in a BMP gene, the method comprising administering to a subject in need, a therapeutically effective amount of an agent that modulates the activity of a BMP gene.